Association Between Adoption of Evidence-Based Treatment and Survival for Patients With ST-Elevation Myocardial Infarction

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Context Only limited information is available on the speed of implementation of new evidence-based and guideline-recommended treatments and its association with survival in real life health care of patients with ST-elevation myocardial infarction (STEMI).

Objective To describe the adoption of new treatments and the related chances of short- and long-term survival in consecutive patients with STEMI in a single country over a 12-year period.

Design, Setting, and Participants The Register of Information and Knowledge about Swedish Heart Intensive Care Admission (RIKS-HIA) records baseline characteristics, treatments, and outcome of consecutive patients with acute coronary syndrome admitted to almost all hospitals in Sweden. This study includes 61 238 patients with a first-time diagnosis of STEMI between 1996 and 2007.

Main Outcome Measures Estimated and crude proportions of patients treated with different medications and invasive procedures and mortality over time.

Results Of evidence based-treatments, reperfusion increased from 66% (95%, confidence interval [CI], 52%-79%) to 79% (95% CI, 69%-89%; $P<.001$), primary percutaneous coronary intervention from 12% (95% CI, 11%-14%) to 61% (95% CI, 45%-77%; $P < .001$), and revascularization from 10% (96% CI, 6%-14%) to 84% (95% CI, 73%-95%; $P<.001$). The use of aspirin, clopidogrel, β-blockers, statins, and angiotensin-converting enzyme (ACE) inhibitors all increased: clopidogrel from 0% to 82% (95% CI, 69%-95%; $P<.001$), statins from 23% (95% CI, 12%-33%) to 83% (95% CI, 75%-91%; $P<.001$), and ACE inhibitor or angiotensin II receptor blockers from 39% (95% CI, 26%-52%) to 69% (95% CI, 58%-70%; $P<.001$). The estimated in-hospital, 30-day and 1-year mortality decreased from 12.5% (95% CI, 4.3%-20.6%) to 7.2% (95% CI, 1.7%-12.6%; $P<.001$); from 15.0% (95% CI, 6.2%-23.7%) to 8.6% (95% CI, 2.7%-14.5%; $P<.001$); and from 21.0% (95% CI, 11.0%-30.9%) to 13.3% (95% CI, 6.0%-20.4%; $P<.001$), respectively. After adjustment, there was still a consistent trend with lower standardized mortality over the years. The 12-year survival analyses showed that the decrease of mortality was sustained over time.

Conclusion In a Swedish registry of patients with STEMI, between 1996 and 2007, there was an increase in the prevalence of evidence-based treatments. During this same time, there was a decrease in 30-day and 1-year mortality that was sustained during long-term follow-up.

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ALTHOUGH RECENT POPULATION-based studies indicate a reduction in incidence, ST-elevation myocardial infarction (STEMI) is still a major health issue worldwide.[1] In a recent study describing the current situation in 30 European countries, the annual incidence for hospital admissions for STEMI varied between 44 and 142 cases per 100 000 inhabitants, which is in keeping with recent data from North America.[2,3]

Over the last 15 years a series of large-scale prospective randomized trials have documented the efficacy and safety of several new treatments available for patients with acute MI. Early reperfusion by mechanical or pharmacological means and adjunctive antithrombotic treatment have been proven to lower mortality.[4,5] There is also trial-based evidence that dual antiplatelet therapy, β-blockers, statins, and angiotensin-converting enzyme (ACE) inhibitors reduce morbidity and mortality in this population.[6-10] Over the

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years, several generations of international and national guidelines have been presented to support the implementation of these evidence-based treatments in clinical practice.[11,12] National and international registries have been introduced to monitor and improve the adherence to current guidelines by continuously providing information on given therapies and outcome.[13-15]

However, only limited information is available on the speed of implementation of these new treatment strategies and its association with long-term survival in real-life health care. The national Register of Information and Knowledge about Swedish Heart Intensive Care Admission (RIKS-HIA) has over the last 15 years recorded baseline characteristics, treatments, and short- and long-term outcomes in consecutive patients admitted to coronary care units in almost all hospitals throughout the country. The aim of the present study was therefore to describe the adoption of new treatments and the related chances of short- and long-term survival in consecutive patients with STEMI in a single country over a 12-year period.

METHODS

The RIKS-HIA database was established as a national quality register in 1995 and includes today all Swedish hospitals (n=72) that include care for acute cardiac diseases. The registry enrolls consecutive patients admitted to a coronary care unit because of symptoms suggestive of an acute coronary syndrome. Information is collected prospectively for more than 100 variables including baseline characteristics, electrocardiographic (ECG) findings, examinations, interventions, and complications in hospital and discharge medication and diagnoses. The whole process has been described elsewhere and the full protocol is available at http://www.ucr.uu.se/rikshia.[13,16] The variables in RIKS-HIA comply with the international Cardiology Audit and Registration Data Standards (CARDS).[17] This study includes all patients in the registry with a first-time diagnosis of MI who presented between 1996 and 2007 with persistent ST-segment elevation detected by ECG at admission.

During the years 1996-2001, the criteria for the diagnosis of acute MI were based on the World Health Organization criteria from 1994[18] combining symptoms, ECG changes, or both with the increase of an biochemical marker (mainly creatine kinase [CK]-MB) exceeding double the upper reference level as the biochemical criterion. The ECG was evaluated for the presence or development of Q-waves, ST-changes, T-wave inversions, or bundle-branch block. From late 2001, the criteria for the diagnosis of MI were adopted according to the European Society of Cardiology/American College of Cardiologists/American Heart Association consensus document, using troponin T or troponin I or eventually 2 CK-MB levels exceeding the 99th percentile in a healthy population together with either typical symptoms or ECG-changes.[19,20] Severe bleeding was defined as a fatal or a cerebral bleeding, or a bleeding requiring surgery or blood transfusion.

Mortality data were obtained by merging the RIKS-HIA database with the National Death Registry, which includes information of the vital status of all Swedish citizens through December 31, 2008. Previous history of stroke, renal failure, chronic pulmonary disease, dementia, cancer, MI, heart failure, and peripheral vascular disease were also obtained by merging with the National Patient Registry, which includes diagnoses for all patients hospitalized in Sweden from 1987 and forward.

To ensure the validity of the information entered into the database a single specially trained monitor visited participating hospitals and compared information in the patient records, including ECG, with the information entered into the RIKS-HIA database involving 30 to 40 randomly chosen patients for each hospital. Data quality has been monitored in 5446 random records from all participating hospitals comprising 299 530 measurements, demonstrating a 95% overall agreement between the registered information and patient records. All patients for whom data were entered into the RIKS-HIA database were informed about their participation in the registry (patients could request to be excluded) and the long-term follow-up. The registry and the merging with other registries was approved by the National Board of Health and Welfare. The Ethics Committee of Uppsala University Hospital approved the study.

Statistical Analyses

If not stated otherwise, data are reported as estimated proportions and medians along with 95% confidence interval (CIs) from random effect models with hospital as random effect and year of hospitalization as fixed effect modeled through a generalized additive models function.[21] The reported *P* values correspond to a linear trend. Developments of estimated proportions of patients treated with different medications and invasive procedures and mortality over time were evaluated by comparing cohorts of patients admitted over 2-year periods both for the whole country and for individual centers. Variations between hospitals are expressed as interquartile range (IQR) and standard deviation with percentage points as unit.

Comparisons of the mortality were also performed by adjusting for differences in baseline characteristics significantly influencing survival and calculating the standardized mortality according to the baseline characteristics in 2007. For each period, standardized mortality was calculated according to a risk score constituted by baseline information based on the 2007-year cohort. Thus, standardized rates can be interpreted as the expected number of deaths that would have occurred if the distribution of baseline and treatment characteristics were the same for all years as in 2007.

Variables in the model were age; sex, diabetes mellitus, hypertension, and smoking; history of MI, stroke, chronic obstructive pulmonary disease, heart

failure, peripheral artery disease, and cancer within 3 years; and medication on admission (aspirin, clopidogrel, β-blockers, statins, other lipid-lowering therapy, warfarin, ACE inhibitors or angiotensin receptor blockers [ARBs], and calcium blockers).

To exclude the possibility that a healthier population at hospitals joining the registry late might have led to lower mortality over time, observed and standardized mortality were also calculated for hospitals participating from the start of the study. Long-term survival was presented as a Kaplan-Meier plot for the each 2-year patient cohorts. All analyses were performed with *R* statistical program version 2.8.1.[22]

RESULTS

During the 12 years, 61 237 patients with STEMI in the registry database fulfilled the inclusion criteria. There was initially an increase in number of sites participating in the registration from 47 sites providing 7152 patients in the first period 1996-1997 to a fairly stable number of 70 to 75 sites with approximately 11 000 patients in the 2-year periods from 1998. Over the observation period, the median age decreased from 71 to 69 years. The proportion of women did not vary (34%-35%; TABLE 1). Hypertension increased from 29% to 39% as did smoking from 27% to 30%, whereas the prevalence of diabetes mellitus remained stable. A history of previous MI decreased from 19% to 10% and a history of heart failure from 6% to 4%.

Of evidence-based in-hospital treatments known to influence outcomes, reperfusion treatment (ie, thrombolysis or primary PCI) showed an increase from 66% to 79%, primary PCI from 12% to 61%, any revascularization (ie, PCI or bypass surgery) within 14 days from 10% to 84% and average use of glycoprotein IIb/IIIa inhibitors from 0% to 55% (Table 1). However, large variations existed between hospitals regarding the speed of implementation of new treatments (FIGURE 1). For reperfusion treatment and primary PCI, the variation did not change over time. For in-hospital coronary angiography, the variation increased to peak in 2002 (IQR range, 45%; SD, 28%) and then decreased thereafter with the smallest variation at the end of the study (IQR, 5.5%; SD, 4.7%). The crude median (25th-75th percentile) time from symptom onset to PCI increased from 185 minutes (120-295 minutes) in 1996-1997 to 216 minutes (137-370 minutes) in 2000-2001 and then decreased to 203 minutes (131-351 minutes) in 2006-2007. Likewise, the crude median (25th-75th percentile) time from onset of symptoms to thrombolysis continuously decreased from 188 minutes (120-315 minutes) in 1996-1997 to 150 minutes (90-276 minutes) in 2006-2007.

The estimated use of aspirin, clopidogrel, β-blockers, statins, and ACE inhibitors or ARBs all continuously increased over the study period, clopidogrel from 0% to 82% (95% CI, 69%-95%; $P<.001$), statins from 23% (95% CI, 12%-33%) to 83% (95% CI, 75%-91%; $P<.001$), and ACE inhibitor or ARB from 39% (95% CI, 26%-52%) to 69% (95% CI, 58%-70%; $P<.001$). Also concerning the implementation of these medications, there was a variation between hospitals (FIGURE 2). For clopidogrel the variation increased to peak in 2002 (IQR, 40%; SD, 23%) and then decreased thereafter with the smallest variation at the end of the study (IQR, 3.4%; SD, 4.4%). The variation decreased from an IQR (SD) of 9.4% (9.0%) in 1996 to 3.7% (3.7%) in 2007 for aspirin, and from an 10.4% (8.7%) in 1996 to 7.0% (4.4%) in 2007 for β-blockers. For ACE-inhibitors and statins the variation remained around the same level throughout the study period.

Over the 12 years, in-hospital complications continuously decreased (Table 1). The estimated proportion of patients experiencing a new MI during hospitalization decreased from 4% at the start of the study period to 1% at the end. Advanced cardiopulmonary resuscitation was performed for 8% in 1996-1997 and in 6% in 2006-2007. Atrioventricular block occurred in 6% and a new atrial fibrillation in 11% in 1996-1997 compared with 3% and 5%, respectively in 2006-2007. The only complication that increased was severe bleedings, which occurred in 1% at the beginning of the study period and in 2% at the end. Patients hospitalized in the latter part of the study period had a shorter hospital stay than those hospitalized early.

From 1996 to 2007 the estimated in-hospital, 30-day and 1-year mortality decreased from 12.5% (95% CI, 4.3%-20.6%) to 7.2% (95% CI, 1.7%-12.6%; $P<.001$), from 15.0% (95% CI, 6.2%-23.7%) to 8.6% (95% CI, 2.7%-14.5%; $P<.001$), and from 21.0% (95% CI, 11.0%-30.9%) to 13.3% (95% CI, 6.0%-20.4%; $P<.001$), respectively. After adjustment for differences in baseline characteristics, a significant reduction in mortality remained with lower standardized mortality over the years (TABLE 2). A similar pattern was seen in a sensitivity analysis that included only hospitals participating from the start of the study (eTable, available at http://www.jama.com). Most of the mortality reduction was seen in-hospital (5.3%) and within the first 30 days (6.4%). However, the long-term mortality was decreasing. Among patients surviving 30 days, the 1 year mortality was reduced by 1.3%. The absolute reduction in mortality was greater in elderly individuals. The crude 1-year mortality decreased from 38% to 27% in patients older than 74 years, from 17% to 9% in patients between 65 and 74 years, and from 7% to 4% in those younger than 65 years. The 12-year survival analyses also showed that the decrease in mortality was sustained over time (FIGURE 3). Based on the survival curves, it could be estimated that the patients admitted in 1996-1997 reached the same cumulative risk as the patients admitted in 2006-2007, 2.7 years earlier.

COMMENT

Few previous studies have characterized recent trends in patient characteristics, treatment, and outcome in the STEMI population. The first finding of

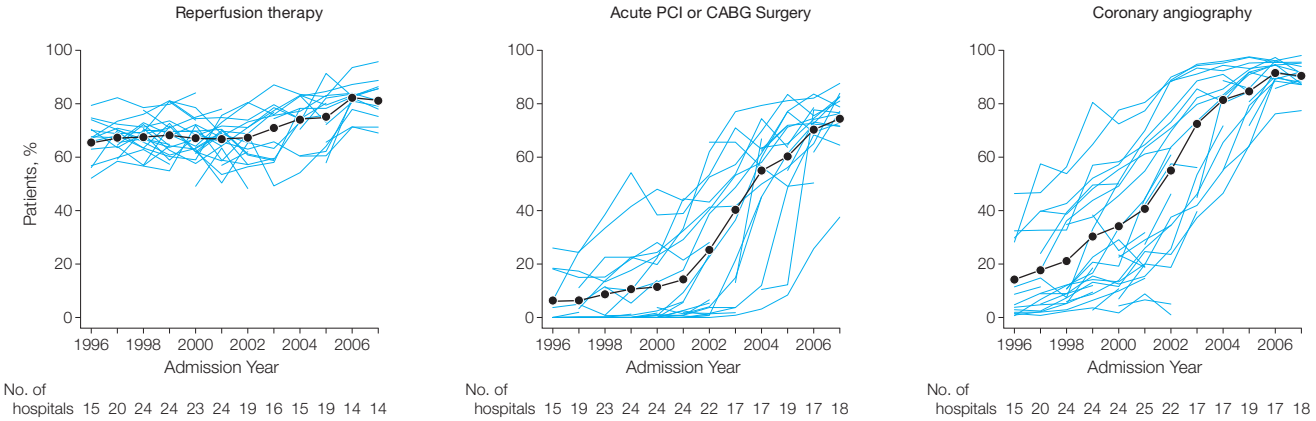
this study, in a nearly complete nationwide cohort of patients with STEMI, is that the adoption of evidence-based and guideline-recommended treatments was gradual. The initial large variation in treatments between hospitals gradually decreased with an increase in equality of care over time. The second finding is that this increase in adherence to treatment guidelines is associated with a gradual lowering of both short- and long-term mortality, which could not be explained by changes in baseline characteristics. From 1996 to 2007, the 30-day mortality has been more than

Table 1. Baseline Characteristics and In-Hospital Course[a]

		Proportion (95% Confidence Interval), %						
	No. of Patients	1996-1997 (n = 7152)	1998-1999 (n = 10 938)	2000-2001 (n = 11 365)	2002-2003 (n = 10 712)	2004-2005 (n = 10 704)	2006-2007 (n = 10 367)	*P* Value
Age, y	61 237	71 (70-71)	71 (70-71)	71 (70-71)	70 (70-71)	70 (70-70)	69 (69-70)	.002
Sex								
Women	61 238	35 (23-46)	35 (27-44)	35 (29-42)	35 (29-41)	35 (27-42)	34 (24-45)	.23
Diabetes	61 238	18 (9-28)	19 (12-25)	19 (14-24)	19 (14-24)	19 (13-25)	19 (11-28)	.14
Hypertension	60 524	29 (18-39)	30 (22-38)	31 (25-38)	33 (27-40)	36 (28-44)	39 (28-50)	<.001
Current smoker	56 576	27 (16-38)	27 (19-35)	28 (22-34)	29 (23-35)	30 (22-38)	30 (20-41)	<.001
Previous disease at entry								
Myocardial infarction	61 238	19 (9-28)	17 (10-23)	15 (10-20)	13 (9-18)	11 (6-16)	10 (4-16)	<.001
Stroke	61 238	9 (2-15)	9 (4-13)	8 (5-12)	8 (5-12)	8 (4-12)	8 (2-14)	.02
Heart failure	61 238	6 (0-12)	6 (2-10)	6 (3-9)	6 (2-9)	5 (1-8)	4 (0-8)	<.001
COPD	61 238	5 (0-9)	5 (1-9)	6 (3-9)	6 (3-9)	6 (3-10)	7 (1-12)	<.001
Peripheral artery disease	61 238	4 (0-9)	4 (1-7)	4 (1-6)	4 (1-6)	4 (1-7)	3 (0-7)	.01
Cancer within 3 y	61 238	3 (0-6)	3 (0-6)	3 (1-5)	3 (1-5)	3 (0-6)	3 (0-7)	.005
Renal failure	61 238	1 (0-3)	1 (0-3)	1 (0-3)	1 (0-2)	1 (0-3)	1 (0-4)	<.001
Medication at entry								
Aspirin	60 670	25 (15-36)	27 (19-35)	28 (21-34)	27 (21-34)	26 (19-33)	24 (14-33)	.03
β-Blockers	60 591	24 (14-34)	26 (18-34)	27 (21-34)	28 (22-34)	27 (20-34)	26 (16-35)	.03
Calcium channel blocker	60 548	14 (6-23)	14 (8-20)	13 (9-18)	13 (9-18)	13 (7-18)	12 (5-20)	.001
ACE-inhibitor or ARB	60 610	9 (3-16)	11 (5-16)	13 (8-17)	15 (10-19)	17 (11-23)	19 (10-28)	<.001
Statin	60 575	5 (0-9)	7 (2-11)	9 (5-13)	11 (7-16)	13 (7-18)	14 (6-22)	<.001
Clopidogrel	60 671	0 (0-0)	1 (0-1)	1 (0-2)	2 (0-4)	3 (0-6)	2 (0-5)	<.001
Reperfusion treatment								
In-hospital thrombolysis	60 998	63 (48-77)	60 (50-69)	51 (42-61)	34 (25-44)	15 (7-22)	3 (0-8)	<.001
Prehospital thrombolysis	60 998	3 (2-4)	4 (2-5)	6 (3-9)	9 (5-13)	7 (3-10)	4 (2-6)	<.001
Primary PCI	60 998	12 (11-14)	13 (11-15)	14 (12-16)	19 (15-23)	37 (28-46)	61 (45-77)	<.001
Angiography only	60 998	1 (0-2)	1 (0-1)	1 (0-2)	1 (0-2)	1 (0-2)	3 (0-7)	<.001
Acute CABG surgery	60 998	0 (0-0)	0 (0-0)	0 (0-0)	0 (0-0)	0 (0-1)	0 (0-1)	<.001
No reperfusion treatment	60 998	34 (21-48)	33 (25-42)	32 (25-40)	32 (24-40)	29 (21-37)	21 (11-31)	<.001
Other in-hospital treatments								
Unfractionated heparin	60 338	27 (15-39)	31 (22-39)	28 (21-36)	22 (15-28)	17 (11-23)	16 (8-24)	<.001
Low-molecular weight heparin	60 338	11 (2-19)	18 (10-26)	25 (17-34)	37 (27-46)	45 (35-55)	40 (26-54)	<.001
Glycoprotein IIb/IIIa inhibitor	50 133	0	14 (9-19)	16 (12-19)	23 (17-30)	41 (31-51)	55 (40-70)	<.001
Coronary angiography	61 238	12 (8-17)	18 (13-24)	30 (23-37)	51 (42-60)	76 (67-85)	93 (86-100)	<.001
Revascularization within 14 d	61 238	10 (6-14)	14 (9-18)	21 (15-26)	38 (29-46)	65 (55-75)	84 (73-95)	<.001
Complications								
New atrial fibrillation	59 850	11 (3-20)	9 (4-13)	7 (4-11)	7 (3-10)	6 (2-9)	5 (1-9)	<.001
CPR	60 248	8 (1-14)	7 (3-12)	7 (4-10)	7 (4-9)	6 (3-10)	6 (1-11)	<.001
Atrioventricular block II or III	60 064	6 (0-12)	5 (2-9)	4 (2-7)	4 (1-6)	3 (0-6)	3 (0-6)	<.001
Reinfarction	58 481	4 (0-10)	4 (0-7)	3 (1-5)	2 (0-4)	2 (0-4)	1 (0-4)	<.001
Severe bleeding	47 141	1 (0-3)	1 (0-3)	1 (0-3)	2 (0-3)	2 (0-4)	2 (0-6)	<.001
Hospitals								
No. of hospitals		47	63	71	72	75	75	
No. of patients per hospital, mean (range)		150 (1-407)	171 (3-529)	158 (5-475)	148 (4-639)	142 (5-494)	137 (467)	
Time of stay, d	61 073	6 (6-6)	6 (6-6)	5 (5-5)	5 (5-5)	5 (5-5)	4 (4-5)	<001

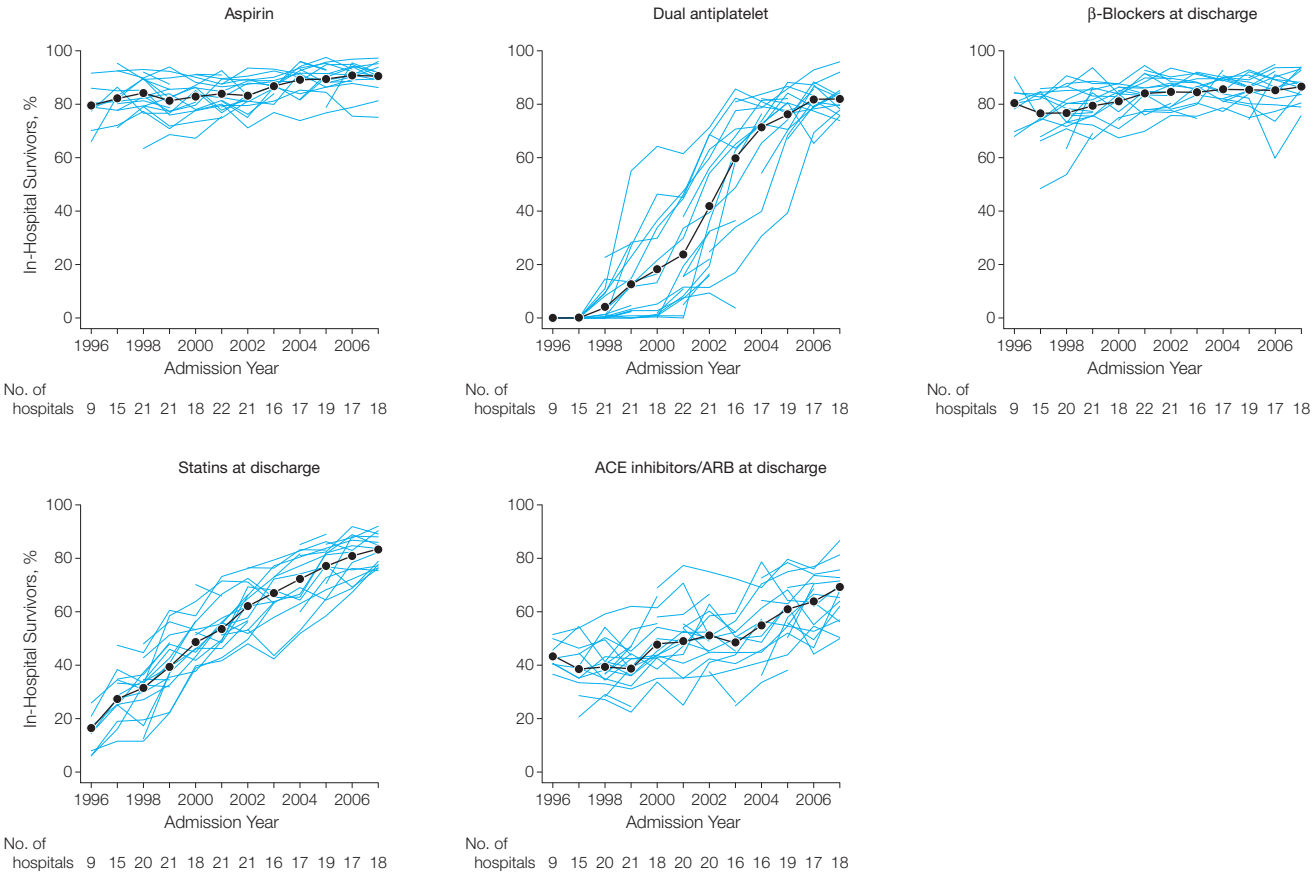
Abbreviations: ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; CABG, coronary artery bypass grafting; CI, confidence interval; COPD, chronic obstructive pulmonary disease; CPR, cardiopulmonary resuscitation; PCI, percutaneous coronary intervention.
[a] If not stated otherwise data are reported as estimated proportions along with 95% CIs from random-effects models.

Figure 1. Crude Proportion of Patients by Hospitals Receiving In-Hospital Treatments



Individual hospitals are shown as blue lines; the aggregated data as the black line. The data markers represent the observed proportions for the aggregated data. Only hospital-years with at least 100 patients are included. CABG indicates coronary bypass graft; PCI, percutaneous coronary intervention.

Figure 2. Crude Proportion of In-Hospital Survivors by Hospitals Receiving Specific Medications



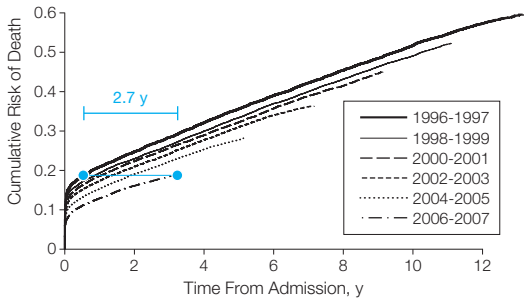
Individual hospitals are shown as blue lines; the aggregated data as the black line. The data markers represent the observed proportions for the aggregated data. Only hospital-years with at least 100 patients are included. ACE indicates angiotensin-converting enzyme; ARB, angiotensin receptor blocker

Table 2. Percentage of Observed (Crude) and Standardized Mortality[a]

	In-Hospital		30-Day		1-Year	
	Observed	Standardized	Observed	Standardized	Observed	Standardized
1996	11.8	10.7	14.2	12.9	20.4	19.0
1997	10.7	10.0	13.6	12.7	19.3	18.2
1998	10.4	9.5	13.2	12.1	18.9	17.7
1999	10.3	9.3	12.3	11.1	17.6	16.4
2000	9.9	8.8	12.4	11.1	17.8	16.3
2001	8.7	7.9	10.7	9.7	16.7	15.4
2002	8.7	7.6	11.3	10.0	16.7	15.1
2003	8.1	7.6	10.0	9.3	15.6	14.8
2004	7.2	6.6	9.1	8.4	13.7	13.0
2005	6.0	5.6	7.8	7.3	12.9	12.2
2006	5.3	5.2	6.6	6.4	10.8	10.8
2007	5.1	5.1	6.3	6.3	11.2	11.2

[a]Standardized mortality is the expected number of deaths that would have occurred if the distribution of baseline characteristics were the same for all years as in 2007.

Figure 3. Long-term Mortality



No. of patients at risk

1996-1997	7152	5381	4856	4364	3907	3454	2173
1998-1999	10938	8430	7661	6895	6216	4159	
2000-2001	11365	8830	8078	7310	4968		
2002-2003	10712	8468	7741	5295			
2004-2005	10704	8663	6055				
2006-2007	10367	6556					

halved with an absolute reduction of almost 8%. The improvements in survival tended to be greater in the latter part of this 12-year period. The third finding is that the 12-year complete follow-up showed that the reduction in mortality is sustained over time. Because the separation between the survival curves tended to increase over time, the improvement of outcome can be expressed as an average gain of at least 2.7 years of life in patients with STEMI in 2007 compared with 12 years earlier. These findings were supported by the reduction of the risk of reinfarction, serious arrhythmias, or cardiac arrest during hospitalization, which is in line with other studies.[23] These changes were associated with only a small increase in severe bleedings as expected by the increased use of interventions and the intensified antithrombotic treatment.

The hospitalization rate for acute MI has slowly declined over the last 15 years.[24] During the same period the proportion of MIs that are STEMIs has decreased, from 47% in 1999 to 23% in 2008 in northern California and from 45% in 1995 to 27% in 2008 in Sweden.[1,13] There have been substantial advances in the treatment of STEMI with the development of more effective thrombolytic agents, the introduction of primary PCI, and improvements in medication by more effective platelet inhibition, β-blockade, ACE-inhibition, and lipid lowering.[11,12]

To improve quality of care and ensure adherence to guidelines, registries on the quality of care representative of the health care systems throughout various countries, such as the Myocardial Ischemia National Audit Project (MINAP) in the United Kingdom, the Acute Coronary Treatment and Intervention Outcomes Network (ACTION) Registry in the United States, and the RIKS-HIA system in Sweden, have been developed.[13-15] Today, RIKS-HIA includes all Swedish hospitals (n=72) admitting patients for care of acute cardiac diseases. The registry therefore provides information on all patients admitted for acute MI in the entire country, their individual baseline characteristics, the use of evidence-based treatments, and the short- and long-term outcome. Simultaneously, all users have continuous access to online interactive reports monitoring the processes of care and outcomes, enabling direct comparisons over time and with other hospitals.[13] National-, regional-, and county-based reports are publicly presented annually. The RIKS-HIA database has thereby stimulated hospitals to improve performance and organize regional systems of care for timely primary PCI, including activation of catheterization laboratories by prehospital electrocardiograms sent from the emergency medical systems.

Although causality cannot be proven, the decrease of in-hospital complications and early mortality likely reflects at least in part the more widespread use of therapies proven in trials to lower the risk of complications and mortality. These improved treatment patterns during this period may play a larger role than changes in patients' baseline characteristics. During the observation period the proportion of patients with previous MI decreased, indicating that the population might have included fewer high-risk patients at the end of the study. This trend has been seen in other studies and may be explained by improved primary and secondary prevention strategies.[25,26] However, after adjustment for baseline characteristics, there was a consistent reduction in short- and long-term mortality. Thus, based on our adjusted statistical analyses, the reduced mortality of patients hospitalized for STEMI seems mainly related to the gradually improved treatment strategies.

Our study demonstrates a large variation in the implementation of new treatments between different hospitals. These large variations, especially regarding coronary angiography during the hospital stay and subsequent dual antiplatelet therapy, were greatest during the start-up of the new treatment modalities, likely reflecting differential rates of adoption of new treatments and decreased gradually over time, which also explains the increase in the proportion of patients reaching the treatment target goals at the end of the study period. However, the large variation in use of ACE inhibitors or ARBs was sustained over time indicating a continuous uncertainty around the indications for these treatments early after STEMI. On the other hand, aspirin, β-blockers, and statins were prescribed with a high degree of agreement throughout the entire study period, although the use of statin treatment was increased over time while the use of the other agents remained stable at a high level. Variations in treatment and deviations from guideline recommendations have negative effects on mortality and morbidity.[27,28] The gradual reduction in variability leading to a high level of guideline adherence might therefore be a key reason for the reduction in mortality. Therefore, identification of undue variations in the processes of care and highlighting areas of need for quality improvement programs are important tasks for the quality registries in health care.[13-15,29]

This study's strengths are that it includes consecutive patients with STEMI covering all patients admitted to hospitals in a nationwide registry over a 12-year period and also provides complete continuing long-term follow-up of 100% of the patients. The study also reflects the full variation day to day in acute coronary care for all incoming patients by including unselected hospitals and regions. The results can therefore be considered representative for the development and results of European acute coronary care of STEMI patients if supported by a continuous quality development program. All data have been prospectively collected, and the validity of the information entered into the database has been tested with 95% agreement between the registered information and patient records.

This study also has limitations. It is an observational study and despite adjustments in the statistical models no causality can be proven concerning the effect of changes of the overall or specific treatment strategies. When analyzing time trends in observational studies, there is always a possibility that other external factors change over time and thereby confound the results. The number of participating hospitals increased from 47 at the start of the study to 75 at the end but remained fairly stable over the last 10 years. A healthier population at hospitals joining the registry late might have resulted in lower mortality over time. However, sensitivity analyses including only hospitals participating from the start did not change the main results. These registry data include only patients entering the hospital, including the in-hospital course, medications at discharge, and follow-up. Accordingly patients deceased before reaching the hospital or not admitted to specialized facilities for acute cardiac care were not included. Patients' dying before reaching the hospital or changes in routines for admission to coronary care units might accordingly have influenced the outcome in the hospitalized patients.

In conclusion, registry-supported implementation of new treatment strategies over 12 years in STEMI patients in Sweden were associated with an increased use of evidence-based treatments, better adherence to treatment guidelines, and reduced variation across hospitals. These gradual changes in practice were associated with a large and sustained reduction in mortality.

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Study concept and design: Jernberg, Svennblad, Lindbäck, Wallentin.
Acquisition of data: Jernberg, Johanson, Held, Wallentin.
Analysis and interpretation of data: Jernberg, Johanson, Held, Svennblad, Wallentin.
Drafting of the manuscript: Jernberg.
Critical revision of the manuscript for important intellectual content: Johanson, Held, Svennblad, Lindbäck, Wallentin.
Statistical analysis: Jernberg, Svennblad, Lindbäck, Wallentin.
Obtained funding: Jernberg, Wallentin.
Administrative, technical, or material support: Jernberg, Johanson, Held, Wallentin.
Study supervision: Jernberg, Wallentin.
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Online Only Material: The eTable is available at http://www.jama.com.
Additional Contributions: This study would not have been possible without the staff of all hospitals participating in RIKS-HIA in Sweden, who enter data on all coronary care unit patients into the registry over the Internet 24 hours a day every day of the year.

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